Madison, Wis
May 23, 1954

Dear Luca:

I am writing now merely to communicate some interesting developments with coli recombination. The more exciting stems from micromanipulation studies with a derivative of your Hfr X a marker stock in another line (28A), F-. These have been going on for some time without much encouragement, but a trick, learned from Salmonella experiments, has now revived the problem. This is simply to use an Hfr selected for high motility (taking care to avert the F- types that often result from the selection procedure) as one parent; the 28A--F- is already non-motile and also morphologically somewhat different. Crosses after about an hour's mixture in Penassay broth show an appreciable fraction of distinctively paired cells, easily recoghized under the microscope as they swim through the medium, and readily isolated with the micromanipulator. A considerable number of these conjugal pairs have been separated. If They have been allowed to disjoin spontaneously, as will usually occur after an hour or two, and the clones from the exconjugants then examined. About half the viable F- exconjugants have segregated the F- parent and Lac+ S^r ~~exconjugants~~ recombinants; the Hfr (motile) exconjugants have so far shown no recombinants, so I think we can assert that there is a polarized fertilization, a gamete nucleus migrating from the Hfr to the F- cell. A few other recombination types have also been noticed, but not systematically searched, so that the zygote frequency approaches nearer to 100% of the conjugants. (The overall rate in the mixture is of the order of 1% and, while counts are impossible, I am confident there are sufficiently numerous pairs to account for the recombination rate). However, there is considerable inviability, especially of the F-exconjugants, possibly due to the manipulation, the fragility of the pairs, or the fact that the parents are diverse strains and may have some intrinsic genetic incompatibility. Also, there is the usual marked bias in favor of the markers from the F- parent, so we must assume rather regular segmental elimination. The present results tell little of this mechanism; Nelson and I have in press, P.N.A.S.,US, June, a little note on the story I have already detailed to you on the constitution of deficient diploids. I am sorry an extra ms. was not at hand to send you, but you already know all about it. Back to pairs: premature separation usually results in inviability; however, the pairs are often separated a considerable distance (1-2 μ) for some time without visible connection, but Kluyver showed some electron micrographs of the predatory stalks of Caulobacter, likewise invisible, and you will recall the "conjugal bridges" of the photomicrograph sent you last year (in which I still have uncertain faith). I have to try some means of putting the pairs under electron microscopy-- perhaps this may be one of the many things left for our collaboration this fall. No special structures are visible prior to disjunction; the cells usually become very closely approximating for a time, but phase microscopy does not discern any connecting organs; the exconjugant cells remain visibly indistinguishable from ordinary vegetative cells. So far, comparable F- x F- combinations have shown no similar pairs, though there is a bit of nondescript clumping. F+ x F- is to be tested tomorrow <u>in re</u> F+conversion if pairs are numerous, recombination if not. The second item concerns Mal$^-$ and $Lp_2{}^r$: you will recall our interest in your stock of W-583, and the finding that it was a mixture of Mal+ $Lp_2{}^s$ and Mal- $Lp_2{}^r$. This is now seen not to be a fortuitous coincidence: the correlation of these traits is almost perfect, through several cycles of mutation and reversion and in several stocks. Some Mal+ lambda-2-resistant types have been found however, but (as Esther has been studying) not allelic with $Lp_2{}^r$. A conceivable explanation is that amylose (or some other product) blocked in Mal-) is the receptor for lambda-2, but this has to be tested. The main importance of this is in transductions with lambda, since the receptor strain must be $Lp_2{}^s$ (this is one means of selecting reversions from $Lp_2{}^r$; superficially it would resemble a joint transduction of two markers!), but one should caution that Mal should always be checked in parent stocks for crosses where this is a critical marker, as has been done in our work as well as your own. This is all for the moment; it has been a lovely, but short spring-- summer almost here. I trustthe plans for your visit are unaltered.

After long procrastination, we have finally had an appropriation for the remodelling of the Genetics building. If at all possible, this work will be done during the summer; if not, it will be postponed till after you visit--our present facilities will be less comfortable, but still usable, while the remodelling work itself would empty the lab. for the interval. In any event, we are prepared for your visit and ofcourse looking forward to it. If we can do anything to facilitate, let me know. Housing is under consideration, but may have to wait your arrival unless something unusual comes up. We will be on campus most of the summer, but during August will be at the Marine Biological Laboratpry, Woods Hole, Mass. If you could manage to get here between Sept. 7-10, it would help in finding housing; if you will be on the east coast the first week in September, perhaps we could all drive back to Madison together.

Yours sincerely,

Joshua Lederberg